PSI-L Isolator Platform

All Processes

Dr. Paul Ruffieux
Consultant

Connecting a World of Pharmaceutical Knowledge
Requirements

Is it possible to have one Isolator for ...

• Filling under aseptic conditions (Grade A)
• Use of isolator technology in ISO8 room (grade D/C)
• Small throughputs for syringe or vial filling
  300 – 70’000 objects per day
• “Standard” Isolator size and system
• A modular system with flexible configurations preferred
• Good automation grade for the core process: decontamination, filling, stoppering, lyo, capping
One Isolator for...

Applications:
• small scale production, startup batch sizes, clinical trial, stability batch, formulation, compounding, stopper refilling, aseptic toxic handling, ...

Environment:
• aseptic conditions
• high potent pharmaceutical ingredients

Packaging formats:
• glass bottle / vial, syringe, medical device, bag, ampoule, other...
The Solution

An adaptable, multifunctional isolator platform
A Large Choice of Possibilities
Scale-up and Production Flexibility

Simple to scale-up the filling capacity or parallel filling of different substances in one cleanroom
Comparsion Filling Line <> PSI-L

Conventional line <> Small scale line

- Air handling units
- Switchboards
- Pneumatics
- $\text{H}_2\text{O}_2$ system
- Piping, cableway
- 3m cleanroom ceiling
- Isolator
- Filling machine
## Fast Track Project

<table>
<thead>
<tr>
<th>Conventional line</th>
<th>Small scale line</th>
</tr>
</thead>
<tbody>
<tr>
<td>large technical area and cleanroom needed</td>
<td>everything inside the smaller cleanroom</td>
</tr>
<tr>
<td>many interfaces to building structure, HVAC, media</td>
<td>only power and compressed air needed</td>
</tr>
<tr>
<td>more equipment's like WFI, steam</td>
<td>air from the room, back to the room with catalytic converter</td>
</tr>
<tr>
<td>long project time line</td>
<td>short delivery time, quick setup</td>
</tr>
<tr>
<td>FAT after 14-20 months</td>
<td>FAT after 9 months</td>
</tr>
<tr>
<td>Ready for media fill 23-33 months</td>
<td>Ready for media fill 12 months</td>
</tr>
<tr>
<td>extensive custom made design and qualification</td>
<td>design docs and qualification follows standards</td>
</tr>
<tr>
<td>high investment cost</td>
<td>low investment cost</td>
</tr>
</tbody>
</table>
Decontamination system SIS700

Integrated $\text{H}_2\text{O}_2$ vaporiser

- Easy to use
- 100 % automatic
- Decontamination SAL $10^{-6}$
- Working chamber < 210 min
Processing of Toxic Products

Filter for aseptic/toxic application
PSI-L Toxic - Airflow

- H13 safe change filter system for return air
- Hand spray gun for washdown
- WFI tapping point
- Drainable gasket for L-flange
- Bottom drain valves
Material Transfer via Airlock

With H$_2$O$_2$ decontamination

- Rapid transfer
- Integrated H$_2$O$_2$ decontamination system
- Grade A, ISO 5 with unidirectional air flow
- Automatic leak test
- Independent control system, air handling and deco-system
- Transfer time >15 minutes
Fast $H_2O_2$ Airlock SARA-L

Enlarged door and chamber

SARA-M (sterility test isolators)

SARA-L (PSI-L smal scale filling platform)
Possibilities for Material Transfer

First setup and material:
• front-door / main chamber

Continuous transfer:
• RTP alpha systems
• Fast $\text{H}_2\text{O}_2$ airlock(s)
• Sterile endless tubing systems
• Small overpressure mousehole(s)

Foto: Getinge
Standard Options

- Non-viable Monitoring stand alone unit
- Integrated particulate counter with isokinetic probe
- Air velocity sensor
- \( \text{H}_2\text{O}_2 \) sensors
- TLV sensor
- Glove stretcher
- Optional Safe-Change filter system

Foto: Bausch + Ströbel
Exchangeable L-Flange
L-Flange with Inflatable Sealing

- Inflatable sealing (red)
- Better cleanability
- Suitable for wash down
- More distance from Isolator to L-flange
- Less problems with tolerance
- NO change for L-flange dimensions
New Inflatable L-Flange Gasket

Detail washdown design
“Ready to Use” (RTU) Material

RTU packaging material

• Ready to use means:
  – washed, sterilized and packed under aseptic conditions
• Stoppers, caps in bags
• Washed, depyrogenated glass bottles in foil
• Sterile syringes in TUBs
• All packaging material needs to be H\textsubscript{2}O\textsubscript{2} resistant
## Small Scale GMP Production Cost Comparison

(3600 2R vial / hour, 1.5m² lyo, isolator)

<table>
<thead>
<tr>
<th>Conventional line</th>
<th>Small scale line</th>
</tr>
</thead>
<tbody>
<tr>
<td>glass vial 0,06 €</td>
<td>RTU vial ~0.35 – 1.50 €</td>
</tr>
<tr>
<td>WFI up to 0.32 € / vial</td>
<td></td>
</tr>
<tr>
<td>tunnel el. power 0.01 € / vial</td>
<td>H₂O₂ &lt;0.001 € / vial</td>
</tr>
<tr>
<td>cleanroom, building</td>
<td>cleanroom, building -30% m²</td>
</tr>
<tr>
<td>technical area needed</td>
<td>NO technical area</td>
</tr>
<tr>
<td>&gt; 6,0 Mio € equipment's</td>
<td>2,5 Mio € equipment's</td>
</tr>
<tr>
<td>engineering company's</td>
<td>low engineering effort</td>
</tr>
<tr>
<td>Requalification of add. Equipment</td>
<td></td>
</tr>
</tbody>
</table>

All data from customers, SCHOTT, Bausch+Ströbel, Stevanato group
Compounding, Formulation Process

- Connection of bulk vessel with L-flange
- Transfer of needed raw materials with RTP, SARA, etc.
- Weighing, Blending
- Disconnection of bulk vessel (no rotating RTP needed)
Sterility Testing Process

- Example with Sartorius pump
- Millipore pump also possible
- More height inside chamber compared to PSI-M

Interchangeable L-Flange with sterility test pump
Small Scale GMP Production

Work process 1-8
Semi Automated Machines

Manual transfer, automated processing steps
Processing of Closed Vials

Manual transfer, automated process steps

1. Closed Vials
   H₂O₂ decontamination

2. Filling through the stopper

3. Laser re-sealing of the stopper

4. Capping

Foto: Aseptic Technologies
Small Scale GMP Production

Manual transfer, process automated
Small Scale Aseptic Bag Filling

max. 600/h 0.5l

Fotos: Harro Hoefliger
Aseptic Bag Filling Process

Harro Hoefliger L-flange with bag filler (aseptic)

• System Dimensions already suitable for L-flange implementation

• Need to discuss bag supply / entry mechanism
  – Suitable for SARA transfer? – most likely, YES
  – Other approaches with manual transfer system (manual unpackings, etc.)

• Need to discuss bag exit approach (mousehole with chute – easy to implement with L-flange approach)
Small Scale Vial, Iyo Process

vial filling
stoppering
lyophilisation
capping
Small Scale vial filling process

Detail vial filling, stoppering, capping machine

Foto: Bausch + Ströbel
Small Scale vial filling process

3600 bulk vials / hour
Small Scale Lyophilisation

- Lab & Pilot freeze dryer process
- Manual loading, unloading operation with frames
- Up to 5 shelves 1.5 m²
- 30 KG ice capacity
- Space saving sliding door inside Isolator
- Optional H₂O₂ gas decontamination system

Foto: Bausch + Ströbel, GEA Lyophil
Medium Scale GMP Production

SARA with 3 PSI-L in line
Small Scale Filling
Filling, laser re-sealing, capping

Foto: Aseptic Technologies, SL1 robot
Small Scale – Closed Vial

Versatile robot line

• One single robotic machine to fill several ready-to-use containers:
  – Closed Vials (filling, laser re-sealing, snap-fit capping)
  – RTF glass vials (filling, stoppering, alu capping)
  – RTF syringes (filling, plungering)

• All containers are supplied and processed in nests
• Easy change of the robot heads

Foto: Aseptic Technologies
Medium Scale Vial, lyo Process
3600 bulk vial filling/hour, 2x 4.5m² lyophilisation with automatic loading - unloading, capping

Foto: Bausch + Ströbel, GEA Lyophil
Freeze Drying, 5+1 Shelves 4.5m²
Small Scale GMP Production

3600 bulk vials / hour with lyophilisation process
Medium Scale Vial Process

3600 bulk vials / hour
Stopper Processor System (Backside)

- Stopper/cap, siliconising, sterilisation, drying
- Sterile transfer of stoppers and caps into endless bags
- Second bag to exit the isolator
- Third bag outside isolator for transport

=> Ready to use for several filling lines in other rooms / buildings
Stopper Bag Filling

Foto: ATEC Steritec GmbH
Small to Medium Scale

Up to 4000 nested syringes / hour
Small Scale GMP Production

Nested syringe filling (front side)

Picture: Bausch + Ströbel
Nested Syringe Filling

Picture: Bausch + Ströbel
Small Scale GMP Production

Backside, incl. TUB unpackaging machine

Picture: Bausch + Ströbel
SKAN AG – Small Scale Filling

Summary

With the modular isolator and the described filling equipment a flexible solution for small scale filling under aseptic, toxic conditions can be realized.

The isolator protects the operator and the environment from hazardous material, which is processed inside. The filling equipment allows with adequate handling by the operator an automated output of 200 up to 70’000 objects per day/batch, depending on the automation grade of the system.

For small batches and clinical trials, modular filling isolators are the best alternative to a traditional clean room concept.
Thank you!

Questions?

info@skan.ch
Dr. Paul Ruffieux
ruffieux.paul@bluewin.ch

Connecting a World of Pharmaceutical Knowledge